UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/575,938	04/13/2006	Jess G. Thoene	TUL5AUSA	7083

270 7590 12/23/2008

HOWSON AND HOWSON
SUITE 210
501 OFFICE CENTER DRIVE
FT WASHINGTON, PA 19034

EXAMINER	
GUDIBANDE, SATYANARAYAN R	

ART UNIT	PAPER NUMBER
1654	

MAIL DATE	DELIVERY MODE
12/23/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/575,938	THOENE, JESS G.	
	Examiner	Art Unit	
	SATYANARAYANA R. GUDIBANDE	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 August 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,12,13,15,28,30 and 32-40* is/are pending in the application.

4a) Of the above claim(s) *2,3 and 13* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4,12,15, 28, 30 and 32-40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/26/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election of group I (claims 1, 2, 3, 4, 12, 13 and 28, 30 and 32), and election of cysteine dimethyl ester (CDME), breast cancer as the elected species of cancer and radiation as the species of cytotoxic agent in the reply filed on 4/10/08 was acknowledged in the office action dated 7/9/08. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Applicant's amendment to claims in the response filed on 8/26/08 has been acknowledged.

Claims 1-4, 12, 13, 15, 28, 30, 32-40 are pending.

Claims 2, 3 and 13 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 4/10/08.

Claims 37-40 have been added as new claims.

Claims 1, 4, 12, 15, 28, 30 and 32-40 are examined on merit.

Any objections and/or rejections made in the office action dated 7/9/08 and not specifically mentioned here are considered withdrawn.

Withdrawn Rejections

Applicant's arguments, see pages 9 and 10, filed 8/26/08, with respect to the rejection(s) of claim(s) 1, 4, 12, 15, 28, 30, 33, 34 and 36 under 35 USC 102(b) have

been fully considered and are persuasive. Therefore, the rejection has been withdrawn. However, upon further consideration, a new ground(s) of rejection is made in view of amendments to claims 1, 4 and 15.

Maintained Rejections

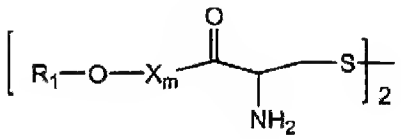
The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 4, 15, 28, 32, 35, 36 and 38 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement as stated in the office action dated 7/9/08. The rejection has been modified and reiterated to reflect the amendments made to the claims 1, 4 and 15 and addition of new claims 38 and 39. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Response to applicant's arguments appears at the end of the reiteration of modified rejection.

Instant invention claims a pharmaceutical composition comprising a compound of the formula,



Wherein 'X' is any naturally occurring amino acid and 'm' is an integer of 0-20 or a pharmaceutically acceptable salt in a pharmaceutically acceptable carrier.

Factors to be considered in making the determination as to whether one skilled in the art would recognize that the applicant was in possession of the claimed invention as a whole at the time of filing include:

a. Actual reduction to practice;
b. Disclosure of drawings or structural chemical formulas;
c. Sufficient relevant identifying characteristics such as:
    i. Complete structure,
    ii. Partial structure,
    iii. Physical and/or chemical properties or
    iv. Functional characteristics when coupled with a known or disclosed correlation between function and structure;
d. Method of making the claimed invention;
e. Level of skill and knowledge in the art and
f. Predictability in the art.

While all of these factors are considered, a sufficient number for a *prima facie* case are discussed below.

The claim as recited claims a composition and with an intended use of treating any and all forms of "cancer" with compounds represented by the above depicted formula. The formula shown above encompass any and all cystine compounds wherein the variable "X" is represented by peptides of length 0 to 20 units composed of naturally occurring amino acids. Over and above the terminal ends are esters of substituted or unsubstituted alkyl chains of 1-10 carbon atoms.

The claim as recited encompasses innumerable compounds. Even with only 20 natural amino acids, i.e., X = any of the 20 amino acids, and for m=20, the number of compounds that the formula as depicted above represents 20^{20} molecules where in the position of each amino acid at position can be any of the 20 naturally occurring residues. Further, inclusion of 'R1" variable as a substituted or unsubstituted alkyl of 1-10 carbon atoms, introduces even more complexity to the molecule. Mere disclosure of a formula

without disclosing representative number of specific examples does not lend adequate written description to the invention. The specification shows only one example, i.e., the elected species CDME in *in vitro* studies of breast cancer cell lines (example 4), toxicity study in example 5 and *in vivo* study of breast cancer cells transplanted in nude mice. Hence, the specification as disclosed does not adequately support the instant invention as recited in the claims to commensurate with the scope of the claims.

Therefore, the claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Response to Arguments

Applicant's argue that the instant specification lists 20 natural amino acids on page 5, lines 5-12 and one of skill in the art would be able to physically prepare different compounds by performing the substitutions of different alkyl groups and substituting one amino acid with another, etc. Applicants further state that "while specification provides one example of treating breast cancer, the specification lists other cancers on page 16, lines 6-14" and one of ordinary skill in the art would be able to perform assay as described in the specification induce apoptosis in a variety of cancer cells.

Applicant's arguments filed 8/26/08 have been fully considered but they are not persuasive.

The issue highlighted in the written description is not about 'how to make the compounds recited in the invention', but the issue is related to "whether applicants are in possession of the invention as recited". Applicants have shown only one specific example, i.e., the elected species CDME and the claims as recited encompasses innumerable number of compounds of varying alkyl chain, modified alkyl chains and peptide of varying length and structural variability. The specification as disclosed does not adequately support the genus of the compounds represented by the formula shown above. Hence, the claims contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

New grounds of Rejections

Claim Objections

Claim 4 objected to because of the following informalities: the variable 'X_s' shown in the formula shown in the claim is not clearly identified and defined. The claim as presented only recites 'X' is selected from the group consisting of D-Asp, ….etc.". Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 28, 30, 32-35 and 37 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 28, 33, 34 and 37 recites the limitation "treatment of cancer or cancer" in the claims as recited. The cancellation of the term “useful for treatment of cancer” in the currently amended claim 1 removed the support for the dependent claims. Therefore, there is insufficient antecedent basis for this limitation in the claims. The base claim 1, from which claims 28, 30, 32-35 and 37 depends from does not recite this limitation "treatment of cancer or cancer" in them. Hence the claim 28, 30, 32-35 and 37 lack antecedent basis.

Claim 36 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 36 recites the limitation "radiation" in line 2. There is insufficient antecedent basis for this limitation in the claim. The base claim 1 from which claim 36 depends from lacks antecedent basis for the limitation.

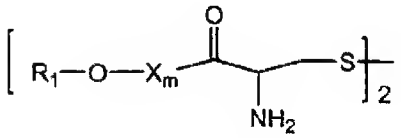
Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

1. Claims 1, 4, 12 and 38-40 are rejected under 35 U.S.C. 102(b) as being anticipated by Bajaj, 1996, The American Physiological Society, 271, F717-F722 in light of McIntyre, 1993, Gut, 34, 386-391.

Instant invention claims a pharmaceutical composition comprising a compound of the formula,



Wherein 'X' is any naturally occurring amino acid and 'm' is an integer of 0-20 or a pharmaceutically acceptable salt in a pharmaceutically acceptable carrier.

Bajaj discloses the composition of with and without 2 mM CDME (the elected species) in 4 mM Sodium lactate, 5 mM alanine, 1 mM butyrate and 7 mM glucose (page F718, beginning of column 2) that was used for incubating proximal tubules to study the importance of phosphate and metabolic substrates produced by cysteine loading (abstract). This reads on claims 1, 4 and 38. The presence of butyrate reads on the instant claim 12 as butyrate is a cytotoxic compound according to the supplemental reference of McIntyre that clearly illustrates that butyrate is cytotoxic (title). Instant claims are drawn to a composition comprising the elected species CDME. Since Bajaj discloses a composition comprising the elected species meeting the limitations of the instant claim it inherently induces apoptosis in a cancer cell and hence reads on the instant claims 38-40.

Hence Bajaj anticipates the instant invention.

2. Claims 1, 4, 15 and 38-40 are rejected under 35 U.S.C. 102(b) as being anticipated by Ben-Nun 1993, The American Physiological Society, 265, F839-F844.

Ben-Nun discloses the composition of 400 μmol CDME (the elected species) in saline or same amount of saline as control (page F840, paragraph 2) administered to rats via injection. This reads on claims 1, 4 and 38. Ben-Nun also discloses that the CDME administration increases the intracellular concentration of cysteine content by 5.65 nmol in blood cells, 0.85 nmol in liver cells and 0.97 nmol in kidney cells (table 1, page F842). This reads on the instant claim 15. Instant claims are drawn to a composition comprising the elected species CDME. Since Ben-Nun discloses a composition comprising the elected species meeting the limitations of the instant claim it inherently induces apoptosis in a cancer cell and hence reads on the instant claims 38-40.

Hence Ben-Nun anticipates the instant invention.

3. Claims 1, 4, 36 and 38-40 are rejected under 35 U.S.C. 102(b) as being anticipated by de Jong, 1996, The Journal of Nuclear Medicine, 37, 1388-1392 in light of the information from the website: http://en.wikipedia.org/wiki/Indium.

de Jong discloses the administration of a composition of 340mg/kg of CDME (the elected species) administered to rats via injection at physiologic pH (page 1389, column 2, paragraphs 1 and 2) in volumes of 200 μL prior to ^{111}In-DTPA-octreotide injection. This reads on claims 1, 4 and 38. The fact that the CDME is administered at physiologic pH into rats clearly illustrates that CDME was in the form of pharmaceutical composition and hence meets the limitations of 1, 4 and 38. Administration of ^{111}In-DTPA-octreotide reads on the limitations of claim 36 as ^{111}In is radioactive in nature. Instant claims are

drawn to a composition comprising the elected species CDME. Since de Jong discloses a composition comprising the elected species meeting the limitations of the instant claim it inherently induces apoptosis in a cancer cell and hence reads on the instant claims 38-40.

Hence de Jong anticipates the instant invention.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Satyanarayana R. Gudibande whose telephone number is 571-272-8146. The examiner can normally be reached on M-F 8-4.30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Satyanarayana R Gudibande/
Examiner, Art Unit 1654

/Andrew D Kosar/
Primary Examiner, Art Unit 1654